# Spatiotemporal Processing of Dynamic Visual Information in the Insect Neural System

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## CONTENTS

## INTRODUCTION

A major task of sensory systems is to supply an organism with knowledge about the dynamics of external stimuli. Thus, much information can be expected to be contained in the temporal structure of their output, the electrical activity of nerve cells. Beyond that, it has been argued that distinct events in the outside world might be encoded by patterns of neural activity, in which the specific timing of electrical signals carries more information than that provided by the overall rate of neural activity (reviews: Borst and Theunissen, 1999; Lestienne, 2001; Shadlen and Newsome, 1994; Tiesinga et al., 2008).

The visual systems of several insect species provide excellent models to study how information about the outside world is encoded by the temporally varying activity of individual nerve cells (review: Egelhaaf and Kern, 2002). A mayor advantage of these model systems is the ability to record neural activity in the unanesthetized state. Moreover, in some insect species, locomotor behavior can be registered in a highly precise way. Such analysis enables the use of dynamic visual stimuli that closely resemble those encountered by the animal in a behavioral context (reviews: Egelhaaf et al., 2005; Kurtz and Egelhaaf, 2003).

In this chapter, some examples of research on dynamic signal processing in the insect visual system will be presented. It will be outlined how the dynamics of brightness and motion signals is encoded into neuronal output signals that are fast and precise enough to form the basis of rapid visuomotor responses, in particular during flight (Taylor and Krapp, 2007). Several examples will demonstrate how individual neurons exploit the spatiotemporal correlations in their visual input to extract behaviorally relevant information, such as the approach of objects (see Section 2) or self-motion-induced panoramic image displacements (see Section 3). As information in the insect visual system is often carried by graded changes of the membrane potential of neurons instead of action potentials (de Ruyter van Steveninck and Laughlin, 1996; Juusola et al., 1995), or by a combination of both (Simmons and de Ruyter van Steveninck, 2005; Warzecha et al., 2003), the synaptic transfer of this type of temporal information will be considered (see Section 3.5).

The last section gives two examples for the role of spike timing in fast sensorymotor control during flight. Section 4.1 outlines how shifts in the position of the horizon in the visual field can be rapidly perceived and used for fast visuomotor control of body attitude during flight. Section 4.2 describes how an essential aspect of motor control during flight, the adjustment of head position by neck motor neurons, depends on the combination of visual motion input with mechanosensory information about the wing-beat cycle.

## FUNCTIONAL SIGNIFICANCE OF TEMPORALLY PRECISE INFORMATION IN THE INSECT VISUAL SYSTEM

During locomotion, in particular when flying, an animal's eye is confronted with rapidly changing brightness signals. From these spatiotemporal patterns of brightness changes, crucial information has to be gathered about the parameters of self-motion, the three-dimensional (3D) layout of the environment, as well as motion of

objects and conspecifics (Britten, 2008; Egelhaaf et al., 2003; Egelhaaf and Kern, 2002; Frost, 2010; Rind and Simmons, 1999). In general, these tasks require fast information processing. However, the biochemical process of photon conversion in the photoreceptor cells (Fain et al., 2010; Yau and Hardie, 2009) results into input signals to the visual system that are per se comparatively slow compared, for example, to sensory signals in the auditory or electrosensory system (Fortune et al., 2006; Grothe et al., 2010; Pollack, 2000). In these sensory modalities, differences in spike timing in the millisecond range or even below can carry information about stimulus localization. In contrast, a general requirement for neuronal interactions in the visual system to be precise on a millisecond or even submillisecond timescale is not immediately evident. Nevertheless, as outlined in Sections 3.3 and 4.1, precisely timed signals occur in the insect visual system and appear to be functionally significant.

The temporal precision at which information is encoded sets limits on how much information is represented, how the code is generated, and how it is read out. In general, spike trains can carry much information if different stimuli reliably lead to millisecond or even submillisecond differences in the timing of individual spikes (reviews: Borst and Theunissen, 1999; Shadlen and Newsome, 1994; Tiesinga et al., 2008). In the visual system, such temporal coding might not be restricted to the encoding of stimulus dynamics. In principle, other stimulus qualities, such as its texture or its position within the receptive field, could also be encoded by different spike patterns. However, unlike a rate code, in which only the number of spikes within a certain time interval is informative, a precise temporal code requires exact mechanisms in downstream neurons to keep track of the temporal structure of spike trains. In the presence of stochastic fluctuations of biophysical parameters, a coarser rate code might thus be more robust and energetically more efficient than a code that relies on precise spike timing (review: Laughlin and Sejnowski, 2003).

Intriguingly, some prominent specializations for fast signaling are present in the visual systems of many insect species. Thus, many insects are far superior to most vertebrates with respect to rapid visual processing and to the execution of visually driven motor responses. First, a phototransduction cascade different from that in vertebrates enables insect photoreceptors to produce fast and brief electrical output signals (Fain et al., 2010; Yau and Hardie, 2009). As a result, the temporal resolving power of insect eyes is often higher than that of vertebrate eyes, as expressed in the high flicker fusion frequencies measured in electroretinograms (Autrum, 1950). Second, sensory input and motor output are often linked by only few processing stages in insect nervous systems. For example, in flies, the motoneurons for the control of head movements are separated from the visual input by only 4–6 synapses (Haag et al., 2010; Huston and Krapp, 2008; Milde et al., 1987). Third, input from the insect visual system is combined with input from other modalities very early during processing (Haag et al., 2010; Huston and Krapp, 2009; Rowell and Reichert, 1986; Simmons, 1980; Strausfeld and Bassemir, 1985). In this respect, insects differ from most higher vertebrates, where such integration is largely restricted to later processing stages. Fourth, several neuropils of the insect visual system contain only a fairly small number of large neurons, which are tailored to their tasks in a highly specific way by their intricate input structure and their distinct biophysical properties (Borst et al., 2010; Gabbiani et al., 2004; Hedwig, 2006; Hennig et al., 2004; Jacobs et al., 2008; Rind and Simmons, 1999;

Simmons, 2002). Such highly specialized neurons, many of which can be individually identified in physiological experiments, are often located close to the sensory input layer. It can be expected that this compact form of neuronal wiring increases processing speed compared to the use of large networks of smaller, less specialized neurons. One prominent example for such a type of neuron is the lobula giant movement detector (LGMD) in the locust brain described in the next section, which is thought to signal object approach on a collision course toward the animal.

## SPATIOTEMPORAL COMPUTATION OF OBJECT APPROACH BY INDIVIDUAL NEURONS IN THE LOCUST BRAIN

### Collision Sensing by Precisely Timed Neuronal Activity in the Locust Brain

The LGMD of locusts presents a prominent example in which a characteristic time course of neuronal activity is selectively triggered by specific spatiotemporal features of the visual input (reviews: Gabbiani et al., 2004; Rind and Simmons, 1999; Rind, 2002; Simmons et al., 2010). In many animals, the visual cues produced by rapidly approaching objects are very effective to trigger a quick escape response (Card and Dickinson, 2008; Fotowat et al., 2009; Fotowat and Gabbiani, 2007; Oliva et al., 2007). The LGMD and its postsynaptic target, the descending contralateral movement detector (DCMD) (see Figure 1a), respond vigorously to objects approaching on a collision course with the animal or their two-dimensional projections, called looming stimuli (O'Shea and Williams, 1974; Schlotterer, 1977; Rind and Simmons, 1992; Rowell, 1971; see Figure 1b).

An important visual cue that may be extracted from a looming stimulus is obtained by calculating the ratio of its angular size and velocity at the retina (see Figure 1c). For an object approaching at constant speed, this ratio is independent of object size and absolute speed, and it decreases linearly as long as the distance of the object is considerably larger than its size (see Figure 1d). Thus, the time course of this ratio provides a useful indicator of whether objects are on a direct collision course, and it enables a good prediction of the time of collision (Lee, 1976). Which combination of object angular size and velocity is best suited to describe the time course of the response of the LGMD/DCMD is currently actively investigated (Gabbiani et al., 1999b, 2004; Rind and Simmons, 1999). Nevertheless, it is clear that these neurons respond specifically to looming objects over a wide range of stimulus conditions (Gabbiani et al., 2001; Rind and Simmons, 1992). The typical response profile is a strong, nonlinear increase in firing rate during object approach. Depending on stimulus conditions, the response either peaks before collision or continues until after collision (see Figure 1b) (Gabbiani et al., 1999a; Hatsopoulos et al., 1995; Rind and Simmons, 1992; Rind, 1996; Rind and Santer, 2004). Much weaker responses or responses that decline much earlier are elicited by other stimuli, for example, stationary objects whose contrast increases over time, translatory object motion, or objects expanding without showing the typical parameter combinations of looming approach (Hatsopoulos et al., 1995; Judge and Rind, 1997; Peron and Gabbiani, 2009; Rind, 1996; Simmons and Rind, 1992).

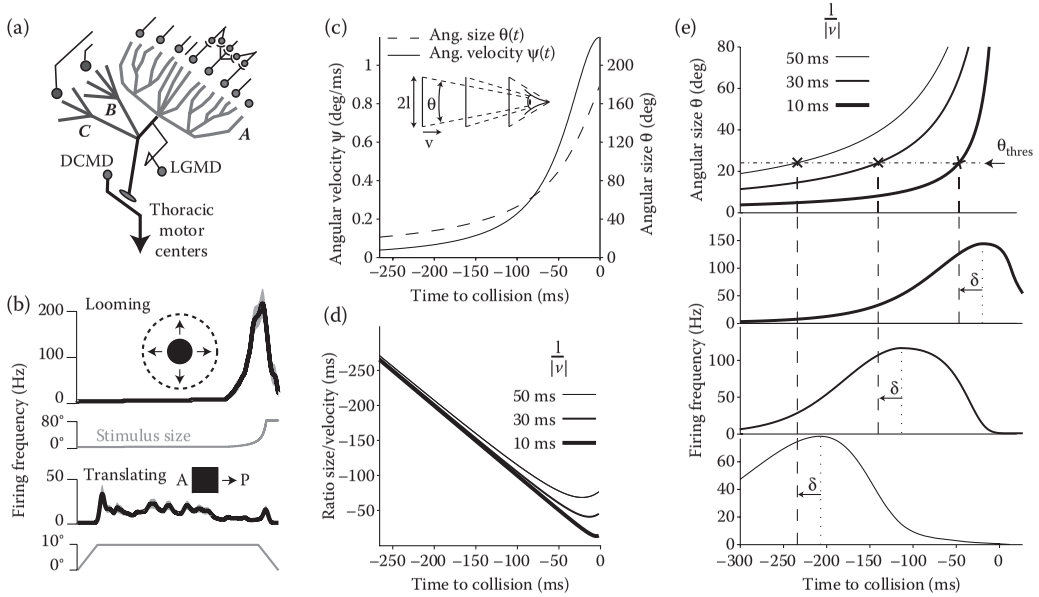


**FIGURE 1** Computation of object approach by individual neurons. (a) Schematic illustration of the locust's collision-sensitive visual interneurons, LGMD and DCMD. The dendritic tree of LGMD consists of three distinct subfields, one of which receives motion-sensitive retinotopic excitatory input (*A*), while two (*B* and *C*) receive phasic inhibition related to object size. (b) Responses of LGMD to a looming disk approaching with $l/|v| = 30$ ms (top; l = radius; v = velocity) and a $10° \times 10°$ square translating from front to back at $10° \text{ s}^{-1}$ (bottom). (c) During the approach of an object on a collision course with constant speed v, both the angle θ subtended by the object and the angular expansion velocity Ψ are nonlinear functions of time during the approach. Example traces for an approach with $l/|v| = 50$ ms. (d) The ratio between angular size and angular velocity for three approaches of different values of the parameter $l/|v|$. (e) Diagram illustrating the time course of angular size θ for three approaches of different values of the parameter $l/|v|$ (top) and of the corresponding neural activity (middle and bottom). Peak firing occurs at a fixed delay (δ) after a certain threshold in the angular size θ has been reached. (Modified from Gabbiani F, Krapp HG, Laurent G. 1999a. *J Neurosci* 19:1122–1141; Gabbiani F, 2002. *Nature* 420:320–324; Peron S, Gabbiani F. 2009. *Nat Neurosci* 12:318–326.)

## Significance of Looming-Sensitive Neurons for the Triggering of Escape Behavior

Apart from the LGMD/DCMD of locusts, neurons that are sensitive to looming stimuli are also present in the nucleus rotundus of pigeons (Sun and Frost, 1998; Wang and Frost, 1992) and in the lobula of crabs (Medan et al., 2007; Oliva et al., 2007). Recently, looming-sensitive neurons were also identified in recordings from the optic lobes and from the neck connective in *Drosophila* (de Vries and Clandinin, 2012; Fotowat et al., 2009). In all these cases, the timing of motor activity generating escape behavior is linked to the response profile of the looming-sensitive neurons (Fotowat and Gabbiani, 2007; Fotowat et al., 2009; Oliva et al., 2007). In one analysis, the response of the LGMD peaked at a fixed delay after the retinal size of the object reached a certain threshold value for a variety of different parameters of the looming stimulus (Gabbiani et al., 1999a) (see Figure 1e). Retinal size might therefore be a critical parameter that triggers an escape response.

In electrical recordings from tethered flying locusts, the temporal integration of inputs from DCMD by a flight motor neuron was characterized (Santer et al., 2006). The recorded motor neuron is thought to have a significant function in controlling escape responses, because it raises the locust's wings and thus initiates an interruption of flight by a gliding phase. The motor neuron only reaches spike threshold when a sufficiently large number of DCMD-mediated EPSPs are integrated, which is the case when DCMD fires a burst of high-frequency spikes in response to a looming stimulus. Intriguingly, the efficiency of DCMD high-frequency spikes to activate the motor neuron depended on the wing-beat phase at which they occur. This dependency was proposed to result from synchronization with a gating input derived from the motor system to ensure that a glide only occurs at the end of a complete wing-beat cycle.

Recently, photoablation experiments showed that DCMD is involved in triggering a precisely timed jump of the locust in response to an impending collision (Fotowat et al., 2011). Using a miniature telemetry system, the activity of DCMD and motor activity was simultaneously registered in freely behaving locusts. DCMD did not play a prominent role in the initial preparatory movements leading to a jump. In contrast, triggering of the jump itself was dependent on DCMD activity. The time course of DCMD firing was a highly relevant parameter for the timely execution of a jump movement, as much of the trial-to-trial variability in jump time could be predicted from the time of the peak of DCMD's firing rate.

## Roles of Spatiotemporal Input Dynamics and Synchronization in the Generation of Looming Sensitivity

The LGMD exemplifies the capacity of single neurons in the insect visual system to perform complex computations. The spatial arrangement and the relative timing of excitatory and inhibitory inputs are crucial for the generation of specific responses to looming stimuli (Gabbiani et al., 2002; Rind and Bramwell, 1996). The LGMD integrates on a large dendrite excitatory retinotopic inputs (Peron et al., 2009; Rind and Leitinger, 2000). Lateral inhibition presynaptic to these inputs may link their strength to retinal image velocity, and reduce their responses to translatory motion

(O'Shea and Rowell, 1975; Rind and Simmons, 1998). In particular, motion was suggested to cause a "critical race" over the dendrites of the LGMD, resulting from the particular arrangement of excitatory and inhibitory input synapses and their presumed latencies (Rind and Bramwell, 1996; Rind and Simmons, 1998). During movement of the edges of an expanding image, excitation arrives before inhibition and wins this race.

Recently, a mechanism that is independent from inhibition was suggested to shape the selectivity of the LGMD for looming stimuli (Jones and Gabbiani, 2010). It was found that a looming stimulus tends to synchronize a large population of synaptic inputs to the LGMD. This is the case because presynaptic neurons are very sensitive to the slope of a luminance change. When stimulating single photoreceptors with luminance changes of equal amplitudes but increasing slopes the peaks of the responses increased and their latencies decreased. These effects were already present in the photoreceptors and became more prominent in downstream processing layers, being strongest in the direct synaptic inputs to the LGMD. The accelerating angular velocity of a looming stimulus stimulates successively activated photoreceptors with increasingly rapid changes in luminance. As a result of the decreasing response latencies, the inputs of the LGMD are synchronized, leading to a large amplitude of the integrated response.

In addition to the mechanisms outlined above, feedforward inhibition plays a role in the generation of looming sensitivity of the LGMD. Two separate dendritic fields arborize in distinct regions of the visual neuropil (see Figure 1a) and receive phasic nonretinotopic, feedforward inhibition related to object size (Rowell et al., 1977). Blocking the latter type of inhibition during object approach increases response strength and delays peak firing time, indicating that it is one of the essential parameters for the generation of a specific response to looming stimuli (Gabbiani et al., 2002).

Recently, it was shown that intrinsic biophysical parameters of the LGMD also contribute to the selectivity of the neuron for looming stimuli. Spike-frequency adaptation, mediated by a calcium-dependent potassium conductance, attenuates the neuronal response to translatory motion, and thus enhances neuronal specificity to looming stimuli (Peron and Gabbiani, 2009). Thus, tuning of the LGMD to looming stimuli is accomplished by a large set of different mechanisms, which build on its synaptic input geometry, the properties of dendritic integration as well as specific intrinsic biophysical characteristics.

## EXTRACTION OF MOTION INFORMATION FROM DYNAMIC VISUAL INPUT IN THE FLY VISUAL SYSTEM

### Correlation-Based Visual Motion Detection

The lobula plate tangential cells (LPTCs) of flies present a class of neurons, which process global dynamic visual input, similar to LGMD and DCMD in locusts (see Section 2). However, unlike LGMD/DCMD, these neurons respond to visual motion in a highly direction-selective way (see Figure 2a). They are excited by motion in their preferred direction (PD), but inhibited by motion in the opposite

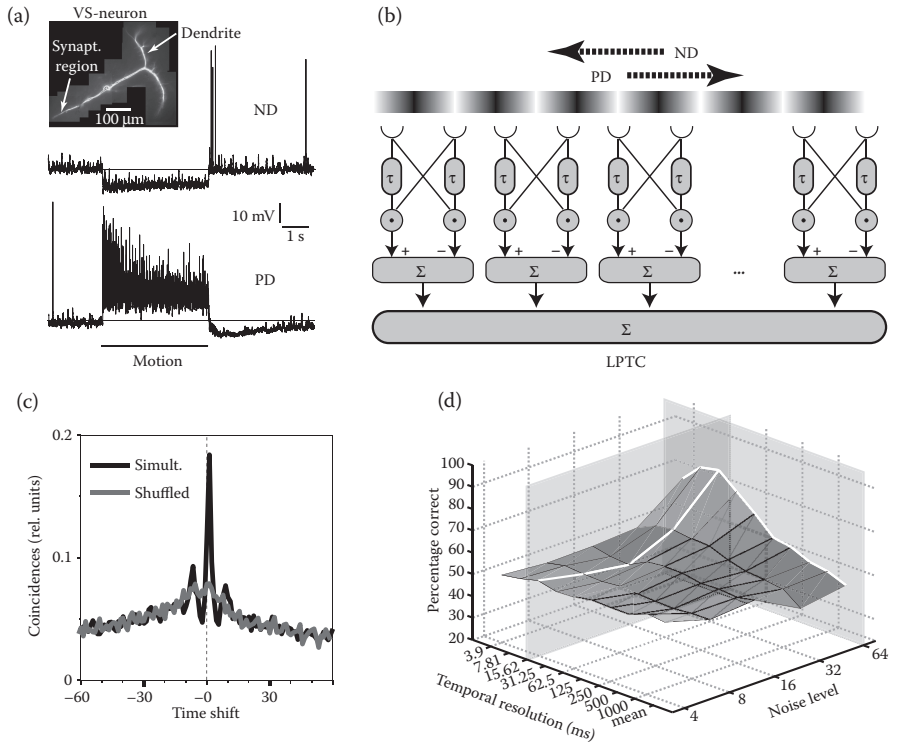


**FIGURE 2** Temporal processing of motion information in the fly visual system. (a) Top, one of the fly's LPTCs, a VS-neuron, visualized after staining with a fluorescent dye. Bottom, responses to motion in preferred direction (PD) and null direction (ND). The responses consist of graded changes in membrane potential and spikes. (b) Computational principle of motion computation. EMDs correlate (by multiplication, "•") the brightness signal from one location in the visual field with a temporally delayed (by a low-pass filter with time constant τ) brightness signal from a neighboring location. Subtraction of the output from one detector half unit from its mirror-symmetric counterpart yields a local motion signal that is positive for motion in PD and negative for motion in ND. Integration over an array of EMDs provides global motion signals. (c) Synchronization of spikes in the fly's H1 and H2 neurons with common synaptic input. Cross-correlogram between the simultaneously recorded responses (black) and cross-correlogram between shuffled responses to the same velocity modulation (gray). (d) Responses of the fly H1 neuron to randomly positioned dots moving in the PD were recorded. Discrimination performance, using an ideal observer paradigm, between traces with different temporal fluctuations in the luminance of dots ("brightness noise"). Different levels of brightness noise and different temporal resolutions of the measure of discrimination were tested. The highest noise level (64) covered the entire available brightness range of the monitor. ((a) Modified from Rien D, Kern R, Kurtz R. 2011. *Eur J Neurosci* 34:705–716.(c) Modified from Warzecha AK, Kretzberg J, Egelhaaf M. 1998. *Curr Biol* 8:359–368; (d) Modified from Grewe J. 2003. *J Neurosci* 23:10776–10783.)

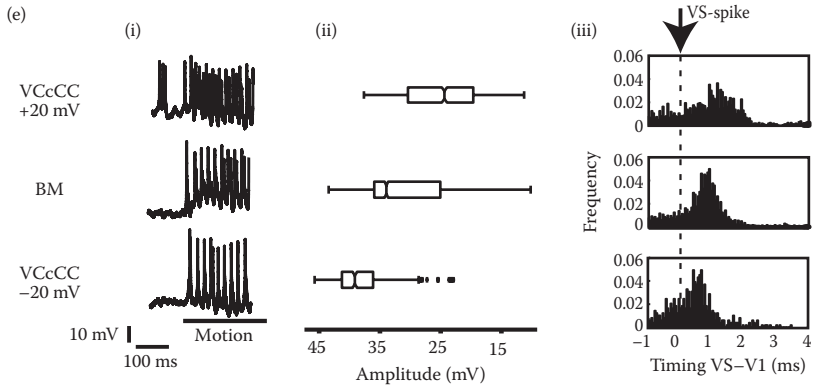


**FIGURE 2** (Continued) (e) Impact of graded changes in membrane potential of a fly VS neuron on spike amplitude and on temporally precise initiation of spikes in the postsynaptic V1 neuron. (i) Responses of VS to motion recorded in bridged mode (BM) and with different graded holding potentials in VCcCC. For these conditions, amplitude of spikes (ii) and histograms of frequency distributions of the latency between spikes in VS and V1 (iii) are shown. ((e) Modified from Rien D, Kern R, Kurtz R. 2011. *Eur J Neurosci* 34:705–716.)

direction, the null direction (ND). The responses of LPTCs to visual stimuli can be monitored by electrical recordings and functional imaging *in vivo* in several genera of fly, in particular *Calliphora*, *Lucilia*, and *Eristalis* (reviews: Borst et al., 2010; Egelhaaf et al., 2005; Kurtz et al., 2008) and, since recently, as well in *Drosophila* (review: Borst, 2009). The detailed analysis of the response properties of LPTCs together with the study of behavioral responses to visual motion provided insight into the basic steps of motion detection, even though these computations are to a large extent carried out further upstream in the visual pathway (reviews: Borst and Egelhaaf, 1989; Borst et al., 2010; Egelhaaf and Borst, 1993; Egelhaaf, 2006). LPTCs integrate the outputs of arrays of numerous local motion-detecting elements, which are too small to be easily accessible to electrical recordings. Thus, LPTCs became a favorite model for the study of the basic mechanisms underlying motion detection and for analyzing the links between neuronal response dynamics and motor control.

There is vast evidence that the computational principle underlying visual motion detection is a type of coincidence detection performed by a so-called elementary motion detector (EMD, see Figure 2b, review: Borst and Egelhaaf, 1989). Some aspects of this type of computation are reminiscent of basic models for sound localization based on interaural time differences (review: Grothe et al., 2010). However, the temporal scale on which coincidence needs to be detected is nearly an order of magnitude shorter in auditory processing than in visual motion computation. In its simplest form, an EMD is organized in the following way. It has two inputs, which are sensitive to the luminance modulations of neighboring locations in the visual field. The signals from these input lines interact in a nonlinear way after one of them is temporally delayed. In EMD models, the nonlinear interaction and the delay are usually implemented as a multiplication and a temporal low-pass

filter, respectively. A moving luminance signal that first arrives at the nondelayed detector input and subsequently at the delayed input will temporally coincide at the multiplication stage if its velocity fits to the detector's delay. By combining two mirror-symmetrical detector units, the outputs of which are subtracted from each other, the EMD yields positive output for one direction of motion and negative output for the opposite direction. In more elaborate implementations of the EMD, additional temporal and spatial filters are added to the basic model (see, e.g., Brinkworth and O'Carroll, 2009; Lindemann et al., 2005). Moreover, EMD models have been proposed that use instead of a formal mathematical multiplication a biophysically more realistic form of coincidence detection, such as a neuronal computation based on shunting inhibition (reviews: Borst and Egelhaaf, 1993; Clifford and Ibbotson, 2002).

## Reliability of Responses to Time-Varying Visual Motion Signals

The retinal image shifts during self-motion, called "optic flow," provide a rich source of information about the parameters of locomotion and about the 3D layout of the environment (reviews: Egelhaaf et al., 2009; Lappe et al., 1999; Taylor and Krapp, 2007). LPTCs integrate local motion cues supplied by EMDs over large parts of the visual field (Krapp et al., 1998; Spalthoff et al., 2010), which is a crucial step in the transfer of visual motion input into output signals for locomotor control (review: Taylor and Krapp, 2007). Therefore, fly LPTCs are likely to play a prominent role in providing the motor system with the specific sensory signals that are required for visually guided flight stabilization, course control, and object detection (Egelhaaf, 1985; Huston and Krapp, 2008; Karmeier et al., 2006; Kern et al., 2005).

The optic flow in a typical behavioral situation, flight in an environment with a complex 3D layout, has complex spatiotemporal characteristics. Rather than flying straight ahead over extended periods of time, the flight trajectories of flies are characterized by frequent changes between mainly translatory locomotion and brief periods of rapid rotation movements, called saccades (Geurten et al., 2010; Schilstra and van Hateren, 1998). These locomotor patterns lead to a highly dynamic structure of the resulting optic flow. Thus, the dynamic response characteristics and the reliability of LPTCs and their synaptic interactions are critical parameters in setting the timescale on which information about time-varying optic flow can be conveyed to the motor areas (Karmeier et al., 2006; Kern et al., 2005).

The reliability of the responses of LPTCs to time-varying motion stimuli has been assessed in numerous studies (de Ruyter van Steveninck et al., 2001; Warzecha and Egelhaaf, 1997, 1999, 2001; Warzecha et al., 1998). In one study, the variability of spike trains of an LPTC in *Calliphora*, the H1 neuron, was compared for motion with constant velocity and motion with randomly fluctuating velocity (de Ruyter van Steveninck et al., 1997). Motion of a random bar pattern was repeatedly presented to count the number of spikes in time windows of different sizes and to calculate the variance across trials. The ratio between the variance and the mean (the Fano factor) was close to one when data for different constant velocities were pooled. In contrast, values much smaller than one were found when random velocity fluctuations

were used. Thus, it was concluded that H1 produces more reliable output signals when stimulated with more natural, dynamic inputs compared to constant inputs. However, these conclusions were later challenged by studies, which demonstrated in the same neuron that both with constant and with dynamic stimulation the variability is similarly low, with Fano factors much smaller than one, apart from conditions that lead to very low spike rates (Warzecha and Egelhaaf, 1999; Warzecha et al., 2000). These conflicting conclusions seemed to result not so much from differences in the data obtained, as from differences in data analysis. De Ruyter van Steveninck et al. (1997) pooled data obtained from different evaluation time windows for constant stimulation, but used only equally sized windows for dynamic stimulation. In contrast, in the later studies, time windows of equal size were used for all conditions (Warzecha and Egelhaaf, 1999; Warzecha et al., 2000).

## Temporal Precision of Visual Motion Computation

In the fly motion vision system, timing of spikes with a precision in the millisecond or even submillisecond range has been observed, but the functional significance of this precision is a controversial issue (Egelhaaf et al., 2001; Lewen et al., 2001; Nemenman et al., 2008; Warzecha et al., 1998). A very precise time-locking of spikes occurs most frequently between synaptically coupled LPTCs (Beckers et al., 2009; Farrow et al., 2006; Horstmann et al., 2000) and between LPTCs that share their sources of synaptic input to a large extent (Warzecha et al., 1998). In the latter case, synchronicity between neurons might be elicited either by certain features of the visual input or by common input noise, or by a combination of both. This question was addressed in dual recordings of a pair of LPTCs, H1 and H2, which resemble each other in their receptive field properties (Warzecha et al., 1998). The responses of these neurons to random velocity fluctuations were synchronized to a large extent, as evidenced by a sharp peak in the cross-correlogram calculated for simultaneously recorded response traces (see Figure 2c). However, when responses of the two neurons to identical stimulus sequences were recorded nonsimultaneously, only a fairly broad peak was found in their cross-correlogram. Two aspects were demonstrated by these findings: First, the biophysical properties of H1 and H2 enable precise spike generation on a millisecond timescale. Second, precise spike timing is mostly elicited by stochastic fluctuations of the activity of input neurons and not by time-locking of spikes to the visual stimulus. Consistent with these conclusions, a recent study indicated that in the H1 neuron, precise spike timing is not a major determinant for the quality of velocity encoding (Spavieri, Jr. et al., 2010).

The visual stimuli encountered by the fly in real life differ considerably from those usually applied under laboratory conditions. First, the luminance under outdoor conditions spans a larger range and can reach higher values compared to the stimulus devices mostly used in laboratory experiments. Second, flies are equipped with nearly panoramic vision and are confronted with panoramic stimuli in real life, but usually not in electrophysiological experiments. Third, in particular during flight, the spatiotemporal dynamics of the visual input differs much from experimenter-designed stimuli. These discrepancies might compromise conclusions drawn from laboratory experiments on the role of spike timing in natural signal encoding.

To overcome these problems, recordings of the H1 neuron were performed outdoors, rotating the fly either in a sinusoidal way (Egelhaaf et al., 2001) or with seminatural rotation dynamics (Lewen et al., 2001; Nemenman et al., 2008). The latter two studies revealed that small differences in spike timing, even down to the submillisecond scale, code for subtle differences in the time course of rotation velocity. This finding should not be misinterpreted to mean that every spike is reproducible on a millisecond timescale. Instead, only certain features of the stimulus waveform lead to spike patterns that are distinct enough to contribute to the overall information conveyed by the spike train. For example, fast transitions in velocity may lead to exceptionally short interspike intervals or to spikes that are particularly precise in their absolute timing.

Even though spike trains of fly visual motion-sensitive neurons could be shown to contain information about their input stimuli at submillisecond resolution (Nemenman et al., 2008), it should be kept in mind that the timing of spikes is to a large extent dominated by noise (Warzecha et al., 1998). This compromises the ability to infer the dynamic properties and the qualitative feature of a stimulus from a single spike train. However, the reliability of fast neuronal computations can be improved when the output of a population of neurons instead of a single neuron is used. This aspect was addressed in a study that combined recordings from individual members of a particular class of fly LPTC with modeling of population coding (Karmeier et al., 2005). The VS ("vertical system") neurons form a class of 10 neurons, which all respond to global visual motion as it occurs during horizontal self-rotation of the fly (Hengstenberg et al., 1982; Hengstenberg, 1982; Krapp et al., 1998). The rotation axes that evoke the largest response are spread along the azimuth, such that individual VS neurons differ in their preferred axis. A Bayesian approach was used to calculate how well global motion about different rotation axes is represented in the population response of the VS neurons (Karmeier et al., 2005). With an integration time as small as 10 ms after response onset, the error for the calculation of this rotation axis of the stimulus was estimated to be less than 10°.

## Impact of Light Intensity and Temperature on Temporal Coding of Motion Velocity Fluctuations

At extremely low light levels, the reliability of the visual system is constrained by the stochastic nature of light, which results into a variable temporal pattern of single photon absorptions in the photoreceptors. In flies, the high light sensitivity of the system under such conditions is preserved in motion-vision. As a consequence, single photon effects were observed in the spike patterns of H1 (Lillywhite and Dvorak, 1981) and were indeed shown to be a limiting factor in particular tasks (de Ruyter van Steveninck and Bialek, 1995). De Ruyter van Steveninck and Bialek (1995) analyzed the responses of H1 to stepwise displacements of a random bar pattern. The performance of H1 to discriminate different step sizes was shown to approach the limits imposed by the optical properties of photoreceptors and photon shot noise. However, over which range of luminance conditions and in which tasks the performance of H1 is limited mainly by the photon noise in the photoreceptor

array rather than by internal sources of noise has been a matter of debate (de Ruyter van Steveninck et al., 2001; Lewen et al., 2001; Warzecha and Egelhaaf, 2001). Grewe et al. (2003) made an attempt to discern how these different noise sources compromise the performance of H1. An approach similar to the "equivalent noise" paradigm commonly used in psychophysics was applied to the responses of H1. The influence of photon noise was emulated by random brightness modulations of dots moving in the PD. The minimal modulation depth that is required to affect the responses of H1 was determined (see Figure 2d). The brightness modulations required to modify the response of H1 in a detectable way were much larger than those estimated to result from photon noise. This discrepancy suggests that at moderate brightness levels, and even more so at daylight, neuronal performance is limited by internal sources of variability rather than by photon noise. This conclusion might be compromised by the fact that fairly long stimulus sequences in the range of seconds were used in the experiments. Thus, these sequences might be distinguished by H1 mainly based on differences in the low frequency range, whereas the strongest disturbance of visual processing by photon noise might be on a much finer timescale. However, inconsistent with this argument, the discrimination performance of the ideal observer paradigm used by Grewe et al. (2003) was best on a timescale as fine as 10–15 ms (see Figure 2d). With a coarser temporal resolution of the ideal observer, information about the fine temporal structure remains unused. On the other hand, owing to the presence of trial-to-trial variability, a resolution finer than 10 ms increases the dissimilarity between responses to one and the same stimulus and deteriorates the performance of the ideal observer. Thus, the optimal temporal resolution of the ideal observer gives an idea on which temporal scale the responses of H1 are most informative about a temporally fluctuating input stimulus. Notably, much longer encoding windows (40–100 ms) were found to optimize information decoding when motion stimuli were used that were self-generated by the fly during tethered flight in a flight simulator under closed-loop conditions (Warzecha and Egelhaaf, 1997). A plausible explanation for the longer time windows is the prevalence of fairly slow transitions in velocity in the stimuli generated by such a procedure.

In a recent study, the response of H1 to random velocity fluctuation was systematically tested at different temperatures and luminance values (Spavieri et al., 2010). An increase in any of these parameters, within the tested range, led to an increase in firing rate. In a previous study, a dependency of spike rate on temperature was already shown to be present under outdoors conditions (Egelhaaf et al., 2001). On the other hand, firing precision increased with luminance, but was unaffected by temperature (Spavieri et al., 2010). Moreover, the information rate and the coding efficiency (i.e., the ratio between transmitted information and total entropy) of H1 increased systematically with firing rate. Surprisingly, these information measures did not increase with firing precision. This finding should not be taken as evidence that firing precision is entirely irrelevant for the H1 neuron. With increased firing precision, the temporal scale of signaling is changed. This became evident in a drastically reduced latency, which might, for example, be important to mediate fast responses to abrupt transitions in motion velocity (see also Warzecha and Egelhaaf, 2000).

## Synaptic Transfer of Dynamic Visual Information

The ability of a neuron to produce precisely timed output is only relevant if this temporal information is transmitted to postsynaptic targets. This issue has been studied in the fly motion vision system by paired recordings from individual, synaptically coupled neurons. The V1 neuron integrates motion input from several VS neurons and conveys this signal to the contralateral brain hemisphere. In a series of studies, V1 and one of its presynaptic VS neurons were simultaneously recorded during visual stimulation (Beckers et al., 2007, 2009; Haag and Borst, 2008; Kalb et al., 2006, 2008; Kurtz et al., 2001; Warzecha et al., 2003). The VS–V1 network has some remarkable features, which are relevant for the interpretation of the experimental results of these studies. First, the VS–V1 connection is most likely formed by mixed electrical and chemical synapses, but it is still unclear to which extent the two types of transmission contribute to signal transfer at individual contact sites (Beckers et al., 2009; Haag and Borst, 2008; Kalb et al., 2006). Second, the VS neurons are themselves interconnected by electrical synapses in a chain-like manner (Haag and Borst, 2004). Third, the synaptic output of VS neurons consists of a mixture of graded membrane potential changes and action potentials (Hengstenberg, 1977; Warzecha et al., 2003). These features—graded (analog) synaptic signaling and electrical coupling—are not just a peculiarity of this particular type of synapse, but have been shown to be widespread phenomena in the insect nervous system, as well as in many brain areas of vertebrates (reviews: Alle and Geiger, 2008; Bloomfield and Volgyi, 2009; Borst et al., 2010; Juusola et al., 2007; Simmons, 2002).

Graded presynaptic depolarization of VS cells was shown to be transferred in a fairly linear way to the postsynaptic V1 cell over a broad range of amplitudes (Beckers et al., 2007; Kurtz et al., 2001). Moreover, the dynamics of synaptic signaling between VS and V1 was analyzed by motion stimulation with random velocity fluctuations (Warzecha et al., 2003) and by voltage-clamping the presynaptic membrane potential with sinusoidal waveforms (Beckers et al., 2007). In a frequency range from the lowest tested values (1 Hz) to about 20 Hz, the response of V1 was found to follow the presynaptic graded input fairly well. Similar observations were made at graded synapses between certain ocellar interneurons in locusts (Simmons and de Ruyter van Steveninck, 2005). However, on a finer timescale, a prominent role of presynaptic spikes of VS neurons in shaping the response of the postsynaptic V1 neuron was demonstrated. First, during visual stimulation, temporal coupling with millisecond precision is found between spikes in VS and V1, even during concomitant strong graded fluctuation of the presynaptic membrane potential (Haag and Borst, 2008; Kurtz et al., 2001; Warzecha et al., 2003). Second, brief depolarizing current pulses injected into a VS neuron are much more effective to elicit a precisely time-locked spike in V1 when they trigger a spike in the VS cell than when remaining just subthreshold (Beckers et al., 2009). A functional role of spikes in synaptic transmission is consistent with experimental as well as model data, which suggest that spikes can amplify responses to fast modulations of an input signal, and may thus be used to sharpen the temporal structure of the neuronal response (Haag and Borst, 1996; Kretzberg et al., 2001a, 2001b).

To further elucidate how graded voltage signals and spikes contribute to synaptic transmission in the fly's visual system, dual recordings of VS and V1 during

visual stimulation were performed during voltage-clamp-controlled current-clamp (VCcCC) (see Figure 2e). This method (Sutor et al., 2003) enables selective voltage clamp of slow fluctuations in membrane potential, that is, of the sustained graded signal component. In contrast, fast signals, in particular spikes, are preserved during VCcCC. Thus, if VCcCC and full voltage clamp of a VS neuron differs in its effect on V1, this difference can be attributed to synaptic transmission of fast signals from VS. It was found that full voltage clamp of a VS neuron caused a stronger reduction in overall spike rate in V1 than blocking only the graded component (Rien et al., 2011). Moreover, the graded component was found to interact with the spike component in controlling the postsynaptic response. The amplitude of VS spikes increased when the graded depolarization during visual stimulation was blocked by VCcCC. Spike amplitude increased even more when a sustained graded hyperpolarization was applied during VCcCC, but it decreased during sustained depolarization (see Figure 2e; see also Hengstenberg, 1977). Most importantly, large presynaptic spike amplitude was associated with a high probability of postsynaptic firing (Beckers et al., 2009) and with a short latency between pre- and postsynaptic spikes (see Figure 2e). These findings demonstrate that at VS–V1 synapses in the fly visual system, spikes function in a graded way rather than representing all-or-non signals, which is commonly accepted to be the major mode of spike-mediated synaptic transmission (but see reviews: Alle and Geiger, 2008; Juusola et al., 2007).

Spike bursts have been shown to carry information about stimulus features or about network states (review: Krahe and Gabbiani, 2004). In the fly V1 neuron, the occurrence of brief bursts, mainly formed by only two spikes ("spike doublets"), appears to depend on the synchronized activity of the presynaptic VS neurons (Beckers et al., 2009). Presumably, synchronization of spiking between the VS neurons leads to nearly simultaneous spike input to V1, which might elicit spike doublets. Blocking presynaptic synchronization by voltage-clamping one of the VS neurons led to a pronounced drop in the rate of "spike doublets" in V1 (Beckers et al., 2009). Spike synchronization between LPTCs might result from common input that is unrelated to the visual signal, as has been shown in paired recordings from H1 and H2 (Warzecha et al., 1998). In VS neurons, a further plausible explanation for spike synchronization is their chain-like electrical coupling (Haag and Borst, 2004). Nevertheless, spike doublets in V1 might carry important information about stimulus features. Since the VS neurons differ in their receptive fields and their preferred optic flow stimuli (Krapp et al., 1998), the occurrence of spike doublets in V1 might signal a close correspondence of stimulus features with the preferences of several of the VS neurons instead of only a single one.

## PHASE LOCKING TO PERIODIC INPUT IN MULTIMODAL NEURONS IN THE INSECT SENSORY-MOTOR SYSTEM

### Precise Spike Timing in the Ocellar Pathway of Locusts

In many flying insects, the ocellar pathway forms a second visual system in addition to the compound eyes (reviews: Krapp, 2009; Simmons, 2002). Built as underfocused single lens eyes, ocelli have only poor spatial resolution. However, they provide input

for a sensory-motor pathway that is very fast because it consists of only very few stages, which are connected by large-diameter axons. Accurate timing of spikes in the ocellar pathway of locusts was recently proposed to be relevant for providing appropriately timed control input to flight muscles (Simmons and van Steveninck, 2010).

The interneuron DNI in the locust brain receives synaptic input from ocellar L-neurons, the second stage in the ocellar pathway, and excites thoracic flight motor neurons (Rowell and Reichert, 1986; Simmons, 1980). Spikes of the DNI neuron were shown to be tightly time-locked to rapid decreases in light intensity (Simmons and van Steveninck, 2010) (see Figure 3a). In response to random modulations in light intensity, the standard deviation of spike times was in the range of only 0.5–1.5 ms, depending on the contrast of the stimulus (see Figure 3b). As spikes were sparse, their timing rather than their rate was concluded to form the relevant information in DNI's output signal. Fluctuations in light intensity during movements of a visual horizon in the ocellar field of view were shown to be effective stimuli that drive DNI spiking (see Figure 3c). DNI responded reliably with a precisely timed spike to every cycle of sinusoidal light modulation when the stimulus frequency was in the range of the locust's wing-beat frequency (see Figure 3d). Thus, the regular nodding movement of the head caused by the wing beat during flight would form an effective stimulus for DNI as long as the horizon is kept in the ocellar field of view. DNI output might therefore represent a control signal that is used for rapid corrections of flight attitude. For an excitatory signal delivered to wing muscles, the precise timing of spikes relative to the wing-beat cycle is critical because the effect of excitation depends on the phase of muscle contraction (Misizin and Josephson, 1987). The tight time-locking of DNI output spikes to the wing-beat cycle might thus be beneficial to maintain steady activation of flight muscles as long as flight attitude is kept stable, and to elicit a prompt corrective change in muscle activation when flight attitude has changed.

DNI receives input from another modality, excitation by wind-sensitive hairs on the head (Simmons, 1980). When air puffs were given in addition to a sinusoidal luminance modulation, the precise time-locking of DNI spikes to the phase of the light stimulus was shown to be largely preserved (Simmons and van Steveninck, 2010). It was hypothesized that the natural fluctuations of air velocity during flight coincide with the fluctuations of light intensity, and might therefore even support time-locking of DNI spikes to the wing-beat cycle. This idea is consistent with an earlier study demonstrating that boosts in air velocity caused by flight movements elicit wing-beat-related spiking in another locust wind-sensitive interneuron (Bacon and Möhl, 1979).

## Spatiotemporal Integration of Visual and Mechanosensory Input in the Fly Neck Motor System

A role of periodic, gating-like signals in the generation of properly timed spike output, functionally similar to the interactions that synchronize the locust's DNI activity to the wing-beat cycle, has been described in the neck motor system of flies (Huston and Krapp, 2009). Some of the fly's neck motor neurons generate spike output only when panoramic retinal image shifts coincide with mechanosensory input (see Figure 3e). In these neurons, spikes are phase locked to the periodic signals produced by mechanosensory organs at the base of the halteres, club-like appendages of dipteran flies

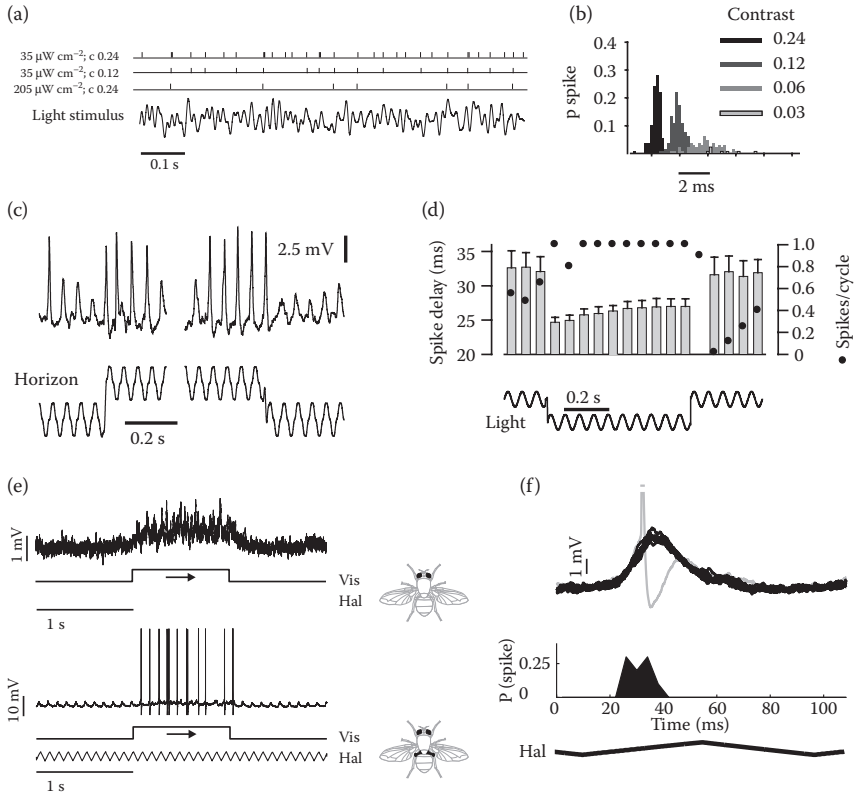


**FIGURE 3** Spike timing in insect sensory-motor systems. (a) Spikes (vertical lines) of the DNI neuron in the locust's ocellar pathway in response to random modulations in light intensity. Different mean intensities and contrasts were tested. (b) Histograms of spiking probability were averaged over 128 repetitions of the same modulated light stimulus (mean intensity 35 µW/cm²). The plot shows a brief instance in time during which a single spike occurred in many of the traces, and illustrates the temporal precision of individual spikes (standard deviation of spike time <0.5 ms at a contrast of 0.24). (c) Responses of DNI to up-and-down movements of a horizon, simulated by dividing a monitor into a top bright and a bottom dark part. An oscillation of the horizon at 20 Hz, which mimics the effect of nodding movement of the locust's head during flight, elicits reliable spiking only when the horizon is shifted upwards above a critical position. (d) Quantification of the reliability and the timing of DNI spikes in response to sinusoidally modulated light that jumped between different mean intensities. (e) Recordings from a neck motor neuron in the blowfly *Calliphora vicina* were performed during visual stimulation with a drifting grating and stimulation of the mechanosensitive haltere system. Visual motion in the PD alone only leads to subthreshold depolarization (top). In contrast, the combination of visual motion and haltere oscillation elicits spikes (bottom). (f) Postsynaptic potentials during haltere stimulation are phase-locked to the cycle of haltere movement (top). During concomitant visual stimulation, this phase-locking results into spikes that occur at a distinct phase of the haltere stimulus (bottom). ((a–d) Modified from Simmons PJ, van Steveninck RR. 2010. *J Exp Biol* 213:2629–2639; (e,f) Modified from Huston SJ, Krapp HG. 2009. *J Neurosci* 29:13097–13105.)

evolutionary derived from hind wings. Functioning like a vibratory gyroscope, halteres sense inertial forces during rapid changes of the body in position or attitude (review: Taylor and Krapp, 2007). Since halteres beat at the same frequency as the wings, the multimodal integration together with the high temporal precision at the level of the neck motor neurons leads to a time-locking of muscle activation to the wing-beat cycle (see Figure 3f). Whether this phase locking has a functional significance similar to that proposed for the locust DNI neuron is not clear. Unlike for flight motor neurons, there is in principle no need for neck motor neurons to provide excitation that is properly phase locked to the wing beat cycle. Thus, the primary function of haltere input to neck motor neurons might be to provide a type of gating. This interaction would ensure that gaze stabilization by optomotor head movements is effective during locomotion, but largely reduced during rest. Consistent with this idea, a distinct bimodality of the head optomotor gain was found on the behavioral level (Rosner et al., 2009). Weak gaze stabilization by pitch movements was closely correlated with haltere rest, whereas much stronger pitch movements were present during haltere activity. Interestingly, in the high-gain condition, oscillations of head movements were present, corresponding in frequency to the haltere beat frequency. These oscillations likely reflect phase locking of spikes of neck motor neurons to the halteres' beat cycle (Huston and Krapp, 2009).

## CONCLUSIONS

The visual system of flying insects presents an excellent case for fast neuronal computation. During flight, processing of spatiotemporal visual information needs to be fast and reliable to enable rapid visually guided locomotor control. In several recent studies, the investigation of visual neurons and motor output has been linked to understand how sensory processing is matched to the properties of its self-generated, continually changing input signals. Such approaches benefit from the slim neuronal architecture and the fairly stereotyped motor patterns of insects, and they emphasize the significance of insects as valuable animal models for the study of dynamic sensory-motor processing. Recent advances in the design of virtual reality stimulation setups and in approaches to monitor neural responses during ongoing locomotor activity, together with the possibility to record from individually identifiable neurons, will in the future further increase our understanding of how the demanding tasks of rapid image processing are solved by tiny insect brains.

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